

REMARKS

The following Remarks address the issues presented in the Final Office Action in the order of their appearance:

Applicant's Related Files and the Kamb Reference:

Applicant's undersigned counsel acknowledges, with regret, the failure to advise Examiner Sisson of Applicant's co-pending applications and to provide Examiner Sisson a copy of the Kamb patent, U.S. Patent No. 5,807,679. The failure to provide the Office with all documents material to the prosecution of the subject application, in a timely fashion, rests entirely with undersigned counsel. The omission, however, was unwitting and caused by a procedural lapse. Counsel is reviewing and revising the internal "related files" handling procedures of his office to ensure that a similar lapse does not occur in the future. Counsel regrets the error.

Rejection of Claims 1-8, 10-12, 14-26, 28, and 29 Under §102(e) in View of Kamb (U.S. Patent No. 5,807,679):

This rejection is respectfully traversed because all of the independent claims in the application, Claims 1, 12, and 19, recite that the fixed portion of the first and second pluralities of primers are different from each other; and (2) each primer in the first and second pluralities also includes a randomized portion. Thus, for example, in Claim 1, the first plurality of primers has a region of fixed sequence "identical to or complementary to" a consensus sequence of interest; the second plurality of primers has an arbitrary region of fixed sequence. In all of the present claims, each primer used includes both a fixed portion and a random portion. It is these two pluralities of primers that are then used to amplify the template DNA.

This approach is distinct from the "island hopping" approach described in Kamb. In Kamb's approach, the primers used in the first round of PCR are fully randomized. The primers are then matched pair-wise and each set of pairs is used to prime a separate PCR

reaction. Some of these PCR reactions generate a single locus of amplified DNA, which the Kamb patent calls "islands." It is the "island" DNA that is then sequenced in preparation for a second round of amplification.

Kamb then performs a second PCR reaction, using primers that are explicitly designed (*i.e.* fully fixed in sequence) to anneal specifically to the "island" DNA and to prime amplification leading from the now-known "island" DNA and into the unknown flanking DNA.

Thus, Kamb's approach requires two distinct amplification steps, separated by a sequencing step: a first PCR using fully randomized primer pairs (to generate the "islands"); sequencing of the "island" DNA; and a second PCR using fully fixed primers designed to anneal specifically to the "island" DNA.

This approach is distinctly different from the present approach, where each primer has a fixed-sequence region and a randomized region. A plurality of these primers is then used to amplify the DNA template. As noted above, Kamb approaches the problem using a first PCR with fully random primer pairs; and then follows the first PCR amplification with a second PCR using primers of fully fixed sequence designed to anneal to the "islands" amplified in the first step.

The success of Kamb's approach relies entirely on generating the initial "islands." Once the "islands" are known, Kamb's approach then proceeds using standard PCR, using primers designed to bind specifically to the "islands." This approach is not the same as that currently claimed, nor does Kamb's approach suggest the present claims.

Applicant therefore respectfully submits that the presently claimed invention is neither anticipated by, nor rendered obvious in view of, the Kamb patent. Therefore, withdrawal of the rejection of Claims 1-8, 10-12, 14-26, 28, and 29 under §102(e) in view of Kamb is respectfully requested.

**Rejection of Claims 1-8, 10-12, 14-26, 28, and 29 for Obviousness-Type Double-Patenting
in View of U.S. Patent N . 6,521,428 B1:**

This rejection is rendered moot by the executed Terminal Disclaimer and Rule 3.73(b)
Certification submitted herewith. Withdrawal of the same is now requested.

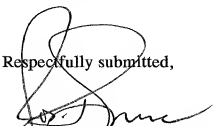
**Rejection of Claims 1-8, 10-12, 14-26, 28, and 29 for Obviousness-Type Double-Patenting
in View of U.S. Patent No. 6,528,288 B2:**

This rejection is rendered moot by the executed Terminal Disclaimer and Rule 3.73(b)
Certification submitted herewith. Withdrawal of the same is now requested.

CONCLUSION

Applicant respectfully submits that the application is now in condition for allowance.
Early notification of such action is earnestly solicited.

Respectfully submitted,


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